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Quercetin Verses Metformin, Comparative Efficacy on the Lipid Metabolism Gene Expression in Different Organs of Diabetic Wistar Rats

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ABSTRACT

Background: Type 2 Diabetes mellitus, is a metabolic disorder responsible for disturbance in carbohydrate, protein and lipid metabolism. The objective of current study was to evaluate the effect of Quercetin and Metformin on serum lipid profile and gene expression involved in lipid metabolism.

Methods: Sixty-four (64) Wistar rats in a range of live body weight 196.75-198.19 grams, were divided in eight (8) groups (n=8 each); CONTROL, DIABETIC, DIAB+MET, DIAB+25Q, DIAB+50Q, NONDIAB+MET, NONDIAB+25Q and NONDIAB+50Q. A single dose of Streptozotocin drug @ 35 mg per kg was used for the induction of diabetes. The particular doses of Metformin and Quercetin were given by gavage on daily basis in their respective groups till the end of 14-week trial.

Result: In case of FAS gene expression in liver, DIAB+MET (1.26±0.03), DIAB+25Q (1.31±0.02) and DIAB+50Q (1.19±0.04), suppresses the elevated expression compared to Diabetic group, while in case of SREBP-1c, both DIAB+MET (1.31±0.05) and DIAB+50Q (1.38±0.04) showed predominant results compared to DIAB+25Q. Moreover, for PPAR-α, DIAB+MET (0.87±0.06) exhibited considerable upregulation in comparison with DIAB+25Q (0.65±0.03) and DIAB+50Q (0.76±0.04). In adipose, FAS gene was significantly downregulated in DIAB+50Q (1.28±0.03) group as compared to other two diabetic treatment groups, however, for PPAR-γ gene, in term of significance both DIAB+MET (0.84±0.05) and DIAB+50Q (0.88±0.06) displayed statistically similar level of upregulation. In muscles, PPAR-α expression was best observed in DIAB+50Q (0.80±0.03) and DIAB+MET (0.76±0.02) compared to DIAB+25Q (0.59±0.03). Moreover, serum lipid profile (TC, HDL, TG, LDL and VLDL) was also significantly improved in Metformin and Quercetin treatment groups. In non-diabetic treatment groups, a non-significant difference was observed when compared to CONTROL group.

Keywords: Diabetes, Lipid, Metabolism, Metformin, Quercetin.

INTRODUCTION

Diabetes, a heterogenous disorder, occurring as a result of environmental and genetic factors, is currently a chronic health issue worldwide (Riddle *et al.,* 2022). Diabetes exists in two major forms: Type 1 Diabetes and Type 2 Diabetes. The type 1 diabetes is basically an autoimmune disorder, involving destruction of pancreatic beta cells due to immune system attacks. This immune response makes the body devoid of insulin, the beta cells hormone accountable for blood glucose regulation. The disease mainly prevails in children but also has a chance of developing in young adult and other age group people. Type 2 diabetes accounting for more than 90% of total diabetes cases (Guo *et al.,* 2023), has a tendency to develop in later stages of life unlike type 1, although now a days owing to the increasing rate of obesity, the disease is also prevailing in young individuals (Olimjonovna, 2024). In this disease type, either the body produce insufficient insulin or becomes insulin resistant (Khajuria *et al.,* 2018; Manikandan *et al.,* 2018; Olimjonovna, 2024), thus failing to manage blood glucose level, which ultimately results in further complications (Devi *et al.,* 2023; Olimjonovna, 2024). The disease is mainly classified by disturbance in fat, carbohydrate and protein metabolism, attributed to dysregulation in insulin action or secretion (Naseem *et al.,* 2020).

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According to 2017 IDF atlas of diabetes, Pakistan is ranked 2nd among 21 countries of Middle East and North Africa for the prevalence of Diabetes, having nearly 7.5 million individuals affected with the disease aged between 20-79, additionally Pakistan is categorized among 21 countries, to be ranked at position 18 based on 6.9% diabetes prevalence (Adnan and Aasim, 2020). The number is expected to reach 16.7 million in 2045, if proper interventional measured were not adopted by the concerned (Bukhsh *et al.,* 2019).

Diabetic dyslipidemia is caused mainly as a result of metabolic disruption and insulin resistance that disturb the lipid metabolism and its related vital enzymes. Diabetes associated dyslipidemia is usually attributed to high serum triglyceride and cholesterol levels, moreover, low levels of HDL-cholesterol. Improving lipid metabolism signifies an important approach towards diabetes treatment. (Rahmani *et al.,* 2023). As plant products are having fewer side effects, interest in anti-hyperglycemic medicines derived from plants has steadily increased in recent years. Now a days, many potential health benefits of polyphenolic compounds, are considered for the treatment of diabetic complications owing to their anti-inflammatory and anti-oxidant properties. Flavonoids (polyphenolic compounds subclass), are known for their beneficial role in lipid metabolism (Umar and Utari, 2019), which is often affected due to prolong untreated diabetes (Kane *et al.,* 2021). Flavonoid also exhibit varied beneficial health effects for diabetes management, *i.e.*, improving insulin sensitivity and secretion along with slowing carbohydrates absorption in intestine. One of the vital flavonoids considered for treating diabetic complications (including dyslipidemia) is Quercetin. A considerable number of research studies are available, focusing on antidiabetic properties of Quercetin and highlighting their importance in relieving diabetic complications (Yan *et al.,* 2023). Quercetin ameliorate lipid associated metabolism and liver injury, moreover its protective effect is also evident from its role in mitigating diabetes related cardiovascular injury (Hosseini *et al.,* 2021), for which the major risk factor being considered is dyslipidemia (Arvanitis and Lowenstein, 2023). The vital regulators of lipid metabolism include genes namely FAS, PPAR-α, SREBP-1c and PPAR-γ, therefore they are used as molecular marker for various metabolic syndrome especially dyslipidemia (Karimi-Sales *et al.,* 2019).

To our best knowledge, there is not even a single study pertaining to comparative anti-dyslipidemia effect of organic product Quercetin and synthetic drug Metformin. The main objective of current research was to compare the anti-dyslipidemia effect of Quercetin and Metformin, in term of gene expression and lipid profile.

MATERIALS AND METHODS

Animal acclimatation

For this particular research, Wistar rats were kept in animal shed of University of Balochistan (Quetta, Pakistan), providing appropriate acclimatization period. To obtain homogenized live body weights, all the rats had free access to food and water, controlled environment with optimal temperature 24±5°C and 12-12 hour of light dark cycle each. Prior trial, experimental rats were allowed to feed on high fat diet (6% cellulose, 12.8% maize starch, 6.6% dextrose, 28.6% casein, 31.1% beef tallow, 9.7% minerals, 1.3% vitamins and 3.9% sun flower oil) for 21 days. The ethical approval for conducting this research was obtained from ethical committee, University of Balochistan.

Animal grouping

· At week 0, sixty-four (64) Wistar rats in a range of live body weight 196.75-198.19 grams, were divided in eight (8) groups (n=8 each). A single dose of Streptozotocin drug (MS07936, Biosynth, Switzerland) @ 35 mg per kg was used for the induction of diabetes. The particular doses of Metformin (Glucophage, Martindow, Pakistan) and Quercetin (Quercetin hydrate, 95%, Thermo Scientific Chemicals, US.) were given by gavage on daily basis in their respective groups till the end of 14-week trial (Naseem *et al.,* 2020).

❖ **CONTROL group**

This group comprised of normal rats (negative control) and were fed on normal diet.

❖ **DIABETIC group**

This group was positive control and consisted of diabetic rats that were fed on normal diet.

❖ **DIAB+MET (Diabetic plus 100 mg/kg metformin)**

In this group, rats were diabetic and were kept on 100 mg antidiabetic metformin drug.

❖ **DIAB+25Q (Diabetic plus 25 mg Quercetin)**

Here, the rats were also diabetic and were provided with 25 mg Quercetin per kg per day.

❖ **DIAB+50Q (Diabetic plus 50 mg Quercetin)**

This group comprised of diabetic rats, kept on 50 mg Quercetin.

❖**NONDIAB+MET (Non-Diabetic plus 100 mg metformin)**

This experimental group included rats that were non-diabetic and were provided with 100 mg metformin drug.

❖ **NONDIAB+25Q (Non-Diabetic plus 25 mg Quercetin)**

This group comprised of non-diabetic rats, kept on 25 mg Quercetin per kg per day.

❖ **NONDIAB+50Q (Non-Diabetic plus 50 mg Quercetin)**

This non-diabetic group was given 50 mg Quercetin.

Extraction of serum

After 14 weeks trial period, blood was collected in vacutainer serum gel collection tubes. Following clotting of blood, these tubes were centrifuged at 2500 rpm for 10 minutes to collect serum, that was stored at -80°C for lipid profiling through micro lab-300 using Innoline commercial kits.

mRNA extraction, cDNA synthesis, real time PCR

The skeletal muscle, hepatic and adipose tissues were isolated from rats, washed with saline water and were stored at -80°C. Following the manufacturer's instructions, Trizol reagent (Bioshop, Canada) was used for the extraction of RNA from the frozen samples of all the three tissues. The commercial RNA extraction kit (CO2203403, Ascend.bio, UK) was used. The extracted RNA was quantified using nanodrop (absorbance at 260 nm). RNA (1 μg) was changed into cDNA by the process of reverse transcription in a reaction volume of total 20 μl using cDNA kit (01317155, Thermo-scientific, Lithuania). The conventional PCR was used for the conversion of RNA into cDNA, involving annealing at 25°C for 5 min, elongation step at 42°C for 60 min and enzyme inactivation at 70°C for 5 min. Quantitative PCR with the aid of SYBR Green master mix (Thermos-scientific) was operated on a Qiagen (Germany) following the instructions given by the manufacturer. The PCR was performed for a total of 45 cycles. The PCR product was monitored continuously by reading the fluorescence throughout the reaction. The gene expression results were analyzed on Rotor gene Q series software. Primer3 website was used for designing the primers. The GAPDH (housekeeping gene) was used for normalizing the mRNA levels. The delta Ct method was used for the relative quantification. The primers used in real time PCR are mentioned in Table 1.

Statistical analysis

Results of the current study are represented as mean ± SEM. One way ANOVA was used for the analysis followed by Duncan multiple range test. Results were analyzed at level of significance (p<0.05), which was considered as significant for the particular study.

RESULTS AND DISCUSSION

Diabetes is regarded as one of the major health concerns worldwide. More than 90% of diabetes cases are attributed to type 2 diabetes mellitus and this particular disease is often ascribed as multifactorial origin chronic metabolic disorder. Diabetes is responsible for disturbing the lipid metabolism and causing inflammation in body. Polyphenols are phytochemicals that are present in vegetables and fruits, moreover they are further categorized into flavonoids, phenolic acids, stilbenes and lignans. Foods rich in Polyphenol and dietary supplements both are linked with a lower occurrence of lipid dependent cardiovascular disease (Costa *et al.,* 2022). A common flavonoid, Quercetin, readily available in vegetables and fruits, is a potent antioxidant. Quercetin exhibit varied beneficial features, namely anti-diabetic, anti-dyslipidemia, anti-inflammatory, anti-cancer and antioxidant properties (Wang *et al.,* 2022). Metformin hydrochloride with its anti-hyperglycemic and anti-dyslipidemia ability is also being in practice for diabetes treatment (Pournaghi *et al.,* 2012; Szymczak-Pajor *et al.,* 2022). Quercetin and Metformin play a crucial role in lipid metabolism through lipid metabolism gene expression. In our study, lipid profiling was done at the end of trial. Gene expression data was also recorded in liver, adipose tissue and skeletal muscles individually at the end of 14 weeks trial after slaughtering the rats.

Ameliorative effect of quercetin and metformin on lipid profile in wistar rats

In blood serum, lipid levels are good indicators of cardiovascular health. It is a well-documented fact that untreated type 2 diabetes mellitus results in elevated levels of LDL, triglycerides, VLDL and also decreased level of HDL, promoting progression to coronary artery diseases. Moreover, the deficiency of insulin in diabetes leads to a variety of irrationalities in regulatory and metabolic pathways, which ultimately results in accumulation of lipids namely TC and triglycerides in diabetic individuals. At the end of 14-week trial, serum was isolated from all the 64 albino rats for biochemical analysis. The results were revealed for serum TC, HDL, TG, LDL-C and VLDL-C (Table 2).

In our research study, streptozotocin induced diabetic group displayed a considerable increase in LDL, VLDL, triglyceride, total cholesterol while a significant decrease in HDL levels as compared to CONTROL group rats. Following 14 week treatment, both Quercetin treated and Metformin treated diabetic rat groups showed a substantial reduction in LDL, VLDL, triglyceride, total cholesterol and elevated levels of HDL (Table 2). Earlier researches have also found improvement in lipid profile following Quercetin and Metformin treatment (Albasher *et al.,* 2020; Ali *et al.,* 2020; Abdelkader *et al.,* 2020; Lai *et al.,* 2021; Hacioglu *et al.,* 2021; Chellian *et al.,* 2022; Hu *et al.,* 2022; Jiang *et al.,* 2022; Rahmani *et al.,* 2023).

Table 1: Lipid metabolism genes and their primer sequences.

Lipid metabolism genes	5′-3′ (Forward primer)	5′-3′ (Reverse primer)
FAS	CGCCGTGGTGCTGGAGATTG	CTTGCCGAGGTTGGTGAGGAAG
SREBP-1c	GGCATGAAACCTGAAGTGGT	TGGGCTTTCACCTGGTTATC
PPAR-α	GAGACCCTCGGGGATCTTAG	CGTCTTGTGTCCTGAGCTTG
GAPDH	TCCCATTCTTCCACCTTTGATGCT	ACCCTGTTGCTGTAGCCATATTCAT
PPAR-γ	CTGACCCAATGGTTGCTGATTAC	GGACGCAGGCTCTACTTTGATC

Abbreviations: FAS: Fatty acid synthase, SREBP-1c: Sterol regulatory element binding protein-1c, GAPDH: Glyceraldehyde-3-phosphate dehydrogenase, PPAR-γ: Peroxisome proliferator-activated receptor-γ, PPAR-α: Peroxisome proliferator-activated receptor-α.

Gene expression of FAS, SREBP-1c and PPAR-α in liver

In liver, FAS gene expression showed a significant difference (p<0.05) between CONTROL (1.03±0.09) and DIABETIC group (1.55±0.03), While other groups *i.e.* DIAB+MET (1.26± 0.03), DIAB+25Q (1.31±0.02) and DIAB+50Q (1.19±0.04) showed a considerable difference (p<0.05) compared to DIABETIC group. In term of significance, all the three treatment groups (DIAB+MET, DIAB+25Q and DIAB+50Q) displayed statistically similar downregulation of FAS gene. There was a significant difference (p<0.05) between CONTROL and treatment groups (DIAB+MET, DIAB+25Q and DIAB+50Q). A non-significant difference was observed between CONTROL (1.03±0.09) and non-diabetic treatment groups; NONDIAB +MET (1.01±0.03), NONDIAB+25Q (1.03±0.05) and NONDIAB+50Q (0.98± 0.04) (Fig 1).

SREBP1-c gene expression in liver, also displayed a substantial difference (p<0.05) between CONTROL (1.05±0.12) and DIABETIC group (2.33±0.03), Whereas the treatment groups with diabetes *i.e.* DIAB+MET (1.31±0.05), DIAB+25Q (1.70±0.02) and DIAB+50Q (1.38±0.04) showed a considerable difference (p<0.05) compared to DIABETIC group. The DIAB+MET and DIAB+50Q groups exhibited major reduction in expression of SREBP1-c gene compared to DIAB+25Q. There was a significant difference (p<0.05) between CONTROL and treatment groups (DIAB+MET, DIAB+25Q and DIAB+50Q). A non-significant difference was observed between CONTROL (1.05±0.12) and non-diabetic treatment groups; NONDIAB+MET (0.96±0.02), NONDIAB+25Q (1.01±0.04) and NONDIAB+50Q (0.98±0.04) (Fig 1).

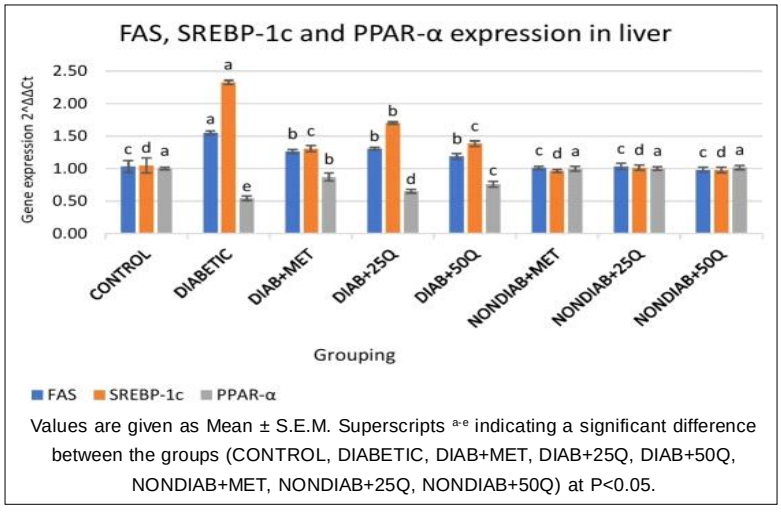
PPAR-α gene expression in liver, revealed a significant difference (p<0.05) between CONTROL (1.00±0.02) and DIABETIC group (0.54±0.04). The diabetic treatment groups *i.e.* DIAB+MET (0.87±0.06), DIAB+25Q (0.65±0.03) and DIAB+50Q (0.76±0.04) showed a considerable difference

Table 2: Lipid profile of Wistar rats in different treatment groups.

Grouping	TC (mg/dl)	HDL-C (mg/dl)	TG (mg/dl)	LDL-C (mg/dl)	VLDL-C (mg/dl)
Control	107.36±3.08^{d}	64.75±1.28^{ab}	97.15±3.37^{d}	23.18±2.62^{d}	19.43±0.67^{d}
Diabetic	213.95±5.17^{a}	32.63±2.14^{d}	224.53±2.94^{a}	136.42±6.34^{a}	44.91±0.59^{a}
DIAB+MET	129.88±3.93^{c}	59.75±2.01^{bc}	144.03±4.75^{c}	41.32±1.65^{c}	28.81±0.95^{c}
DIAB+25Q	165.05±1.86^{b}	54.13±3.96^{c}	176.89±6.94^{b}	75.55±3.69^{b}	35.38±1.39^{b}
DIAB+50Q	137.98±2.42^{c}	67.50±0.85^{a}	132.28±4.85^{c}	44.02±2.46^{c}	26.46±0.97^{c}
NONDIAB+MET	98.28±1.40^{d}	62.75±1.19^{ab}	89.04±3.12^{d}	17.72±1.71^{d}	17.81±0.62^{d}
NONDIAB+25Q	106.58±2.48^{d}	61.00±2.41^{ab}	92.16±3.48^{d}	27.14±2.16^{d}	18.43±0.70^{d}
NONDIAB+50Q	104.78±2.22^{d}	66.50±1.43^{a}	91.79±1.80^{d}	19.92±2.46^{d}	18.36±0.36^{d}

Values are given as Mean ± S.E.M. Superscripts $^{a-d}$ indicating a significant difference between the groups (CONTROL, DIABETIC, DIAB+MET, DIAB+25Q, DIAB+50Q, NONDIAB+MET, NONDIAB+25Q, NONDIAB+50Q) at P<0.05. TC (Total Cholesterol), TG (Total triglyceride), HDL-C (High Density Lipoprotein-Cholesterol), VLDL-C (Very Low-Density Lipoprotein-Cholesterol) and LDL-C (Low Density Lipoprotein-Cholesterol).

CONTROL; Normal group, DIABETIC; Diabetic group, DIAB+MET; Diabetic with 100 mg Metformin treatment, DIAB+25Q; Diabetic with 25 mg Quercetin treatment, DIAB+50Q; Diabetic with 50mg Quercetin treatment, NONDIAB+MET; Non-diabetic with 100 mg Metformin treatment, NONDIAB+25Q; Non-diabetic with 25 mg Quercetin treatment, NONDIAB+50Q; Non-diabetic with 50 mg Quercetin treatment.



Values are given as Mean ± S.E.M. Superscripts $^{a-e}$ indicating a significant difference between the groups (CONTROL, DIABETIC, DIAB+MET, DIAB+25Q, DIAB+50Q, NONDIAB+MET, NONDIAB+25Q, NONDIAB+50Q) at P<0.05.

Fig 1: Gene expression of FAS, SREBP-1c and PPARα in liver.

(p<0.05) compared to DIABETIC group, showing an improvement in liver PPAR-α gene expression compared to DIABETIC. The DIAB+MET group showed relatively better expression of PPAR-α gene compared to the other two diabetic treatment groups. A non-significant difference was observed between CONTROL (1.00±0.02) and non-diabetic treatment groups; NONDIAB+MET (1.00±0.04), NONDIAB+25Q (1.00±0.03) and NONDIAB+50Q (1.02±0.03) (Fig 1).

Gene expression of FAS and PPAR-γ in adipose tissue

In adipose tissue, FAS gene expression showed a significant variation (p<0.05) between CONTROL (1.01±0.06) and DIABETIC group (2.13±0.05), While other groups *i.e.* DIAB+MET (1.40±0.04), DIAB+25Q (1.72±0.04) and DIAB+50Q (1.28±0.03) showed a significant difference (p<0.05) compared to DIABETIC group. The most considerable downregulation of FAS gene was observed in DIAB+50Q group. There was a significant difference (p<0.05) between CONTROL and treatment groups (DIAB+MET, DIAB+25Q and DIAB+50Q). A non-significant difference was observed between CONTROL (1.01±0.06) and non-diabetic treatment groups; NONDIAB+MET (0.99±0.02), NONDIAB+25Q (1.01±0.03) and NONDIAB+50Q (0.97±0.03) (Fig 2).

PPAR-γ gene expression in adipose, displayed a substantial difference (p<0.05) between CONTROL (1.11±0.18) and DIABETIC group (0.33±0.05), Whereas the treatment groups with diabetes *i.e.* DIAB+MET (0.84±0.05), DIAB+25Q (0.61±0.03) and DIAB+50Q (0.88±0.06) showed a significant difference (p<0.05) compared to DIABETIC group. A non-significant difference was observed between CONTROL (1.11±0.18) and non-diabetic treatment groups; NONDIAB+MET (1.15±0.04), NONDIAB+25Q (1.12±0.05) and NONDIAB+50Q (1.17±0.06) (Fig 2).

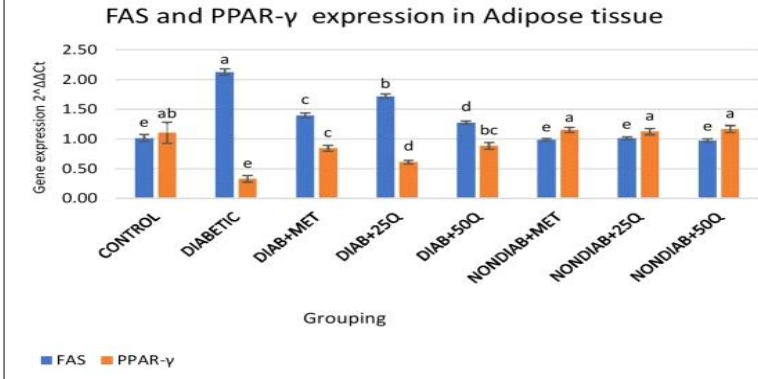
Gene expression of PPAR-α in skeletal muscles

PPAR-α gene expression in skeletal muscle, showed a significant variance (p<0.05) between CONTROL (1.00±0.03) and DIABETIC group (0.39±0.02). The diabetic treatment groups *i.e.* DIAB+MET (0.76±0.02), DIAB+25Q (0.59±0.03) and DIAB+50Q (0.80±0.03) showed a substantial difference (p<0.05) compared to DIABETIC group, indicating an improvement in skeletal muscle PPAR-α gene expression compared to DIABETIC. The DIAB+MET and DIAB+50Q groups showed similar upregulation of PPAR-α gene, with no significant difference between the two groups. A non-significant difference was observed between CONTROL (1.00±0.03) and non-diabetic treatment groups; NONDIAB +MET (1.01±0.02), NONDIAB+25Q (0.98±0.03) and NONDIAB+50Q (1.03±0.03) (Fig 3).

The expression data of PPAR-α in our study is similar with previously reported studies (Karimi-Sales *et al.,* 2019; Malinska *et al.,* 2019; Ting *et al.,* 2018). PPAR-α is disseminated in several body tissues but is mainly present in liver, adipose and skeletal tissues. PPAR-α is involved in gene regulation specifically genes concerned with lipoprotein metabolism, lipid transport and fatty acid oxidation (Małodobra-Mazur *et al.,* 2024).

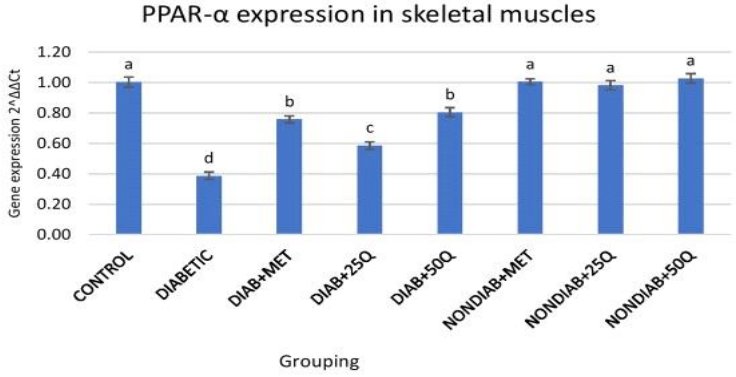
In term of PPAR-γ expression, the findings for Quercetin (Sun *et al.,* 2015) are in line with previous studies. The experimental outcome of our study for PPAR-γ are also in accordance with previous study reporting an upregulation mediated by flavonoid (Singh *et al.,* 2018). Matsukawa *et al.,* 2015, also found a significant upregulation of PPAR-γ in diabetic mice after treatment of mice with flavonoid, which is in accordance with our study results. PPAR-γ is regarded as the adipogenesis master regulator, as it increases the storage of lipid. PPAR-γ is also responsible for regulation of the change from glycolytic state to oxidative muscle fibres (Montaigne *et al.,* 2021).

SREBPs role in lipid metabolism is multifunctional and thereby numerous metabolic issues are related to dysregulation of SREBP for example dyslipidemia, type 2 diabetes, atherosclerosis and fatty liver disease (Li *et al.,* 2023). SREBP-1c is a vital protein responsible for



Values are given as Mean ± S.E.M. Superscripts [a-e] indicating a significant difference between the groups (CONTROL, DIABETIC, DIAB+MET, DIAB+25Q, DIAB+50Q, NONDIAB+MET, NONDIAB+25Q, NONDIAB+50Q) at P<0.05.

Fig 2: Gene expression of FAS and PPAR γ in Adipose tissue.



Values are given as Mean ± S.E.M. Superscripts [a-d] indicating a significant difference between the groups (CONTROL, DIABETIC, DIAB+MET, DIAB+25Q, DIAB+50Q, NONDIAB+MET, NONDIAB+25Q, NONDIAB+50Q) at P<0.05.

Fig 3: Gene expression of PPAR-α in skeletal muscles.

synthesizing fat and when SREBP-1c is activated then it further enhances adipogenic genes transcription such as fatty acid synthase and acetyl-CoA carboxylase, thus accelerating hepatic fat production (Gan *et al.,* 2024). In case of gene expression involving SREBP-1c, Lee and Kim (2022) also found results relevant with out findings, reporting a down regulation of SREBP-1c in Quercetin treated groups in high fat diet model. Pengnet *et al.* (2022), also presented a relatable result, showing a downregulation of SREBP-1c in rats after flavonoid treatment. Karimi-Sales *et al.* (2019), presented a similar result, a downregulation of SREBP-1c in wistar rats following flavonoid treatment which is a similar trend as in our study.

Our study outcome for FAS expression is in accordance with previously conducted studies (Afarin *et al.,* 2024; Lee and Kim 2022). Fatty acid is synthesized by FAS in liver (Sahin *et al.,* 2021) and other tissues namely adipose and skeletal muscle. In diabetes, there is an evident rise in FAS expression and thus consequently leading to dyslipidemia, as FAS is involved in lipid synthesis (Fang *et al.,* 2024). In our study, diabetes induction also causes upregulation of FAS at a considerable level thereby affecting lipid metabolism while treatment with Quercetin and Metformin downregulated the FAS gene.

CONCLUSION

Our study outcome clearly showed that Quercetin flavonoid is equally effective in ameliorating lipid profile and its related gene expression as Metformin which is a synthetic drug. Moreover, the higher dose of 50 mg Quercetin showed comparatively better results in term of lipid profile and gene expression as compared to 25 mg dose.

Conflict of interest

All authors declared that there is no conflict of interest.

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